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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/943,780	08/30/2001	Kevin P. Baker	P2548P1C10	2570

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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	PAPER NUMBER
1643	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/943,780	BAKER ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 24 October 2007 has been entered.

2. Claims 1-26 and 35-36 are cancelled.

3. Claims 27-34 are pending and under consideration.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. This office Action contains New Grounds of Rejections.

Rejections Withdrawn

6. The rejection of claims 27-34 under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility is withdrawn in view of the New Grounds of Rejections below.

7. The rejection of claims 27-34 under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, one skilled in the art clearly would not know how to use the claimed invention is withdrawn in view of the New Grounds of Rejections below.

Rejections Maintained

8. The rejection of claims 27-34 under 35 U.S.C. 102(b) as being anticipated by Bostein et al (WO 99/35170, published 7/15/1999) is maintained.

Applicants' argue that the present application is entitled to the filing date of priority application 60/113,296, i.e., 12/22/1998, which discloses the PRO357

polypeptide and amino acid sequence as well as the gene amplification experiment described in Example 28 of the present specification is described in Example 2 of the '296 application. According to applicant, for the reasons discussed in the reply filed 10/24/2007, description of the gene amplification in the '296 application satisfies the utility and enablement requirements for the PRO357 polypeptide. This has been fully considered but is not found persuasive for the following reasons.

Under 35 U.S.C. 120, the claims in a U.S. application are entitled to the benefit of the filing date of an earlier filed U.S. application if the subject matter of the claim is disclosed in the manner provided by 35 U.S.C. 112, first paragraph in the earlier filed application. Under 35 U.S.C. 119 (a) or (e), the claims in a U.S. application are entitled to the benefit of a foreign priority date or the filing date of a provisional application if the corresponding foreign application or provisional application supports the claims in the manner required by 35 U.S.C. 112, first paragraph. A deficiency under 35 U.S.C. 101 also creates a deficiency under 35 U.S.C. 112, first paragraph. In view of the deficiencies under 35 U.S.C. §§ 101 and 112, First Paragraph set forth below, the claims are not entitled to the benefit of the filing date of the earlier filed applications. Accordingly, the effective filing date for the claimed invention is 8/30/2001, which is the filing date of the instant application and the rejection is maintained.

New Grounds of Rejections

35 U.S.C. §§ 101 and 112, First Paragraph

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 27-34 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific, and substantial asserted utility or a well established utility.

10. Claims 27-34 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific, and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

A portion of the basis for these rejections as previously set forth is withdrawn. Specifically, the examiner no longer asserts that **mRNA levels** are not predictive of polypeptide levels. Therefore, the following references are no longer being relied upon to support the rejections: Haynes et al, Gygi et al, Lian et al, Fessler et al, LaBaer, Chen et al, Hanna et al, Greenbaum et al, Winstead et al, Irving et al, ect. The following references cited and discussed by Applicant pertaining to the mRNA/polypeptide correlation issue will no longer be addressed: Scott Declaration, Polakis Declarations, Futcher et al., Alberts and Lewin, Meric et al., Zhigang et al., ect. The basis of the instant rejections is solely that **gene amplification levels** are not predictive of mRNA or polypeptide levels.

In the interest of clarity, the basis of the rejection is set forth here:

The claims are directed to isolated polypeptides comprising the amino acid sequence of SEQ ID NO:69 with or without its signal peptide, or the amino acid sequence of the full-length coding sequence of the cDNA deposited under ATCC accession number 209527, wherein the nucleic acid encoding said polypeptide is disclosed amplified in lung and colon tumor cells. It is noted that the finding that the nucleic acid encoding said polypeptide is amplified in lung or colon tumor cells is not an activity limitation for the claimed polypeptides; rather, it is a characteristic of a nucleic acid. In other words, the claims do not require that the claimed polypeptides be overexpressed in any tumor, or have any biological activity. Claims are also presented

to chimeric proteins comprising the aforementioned polypeptides. The specification discloses the polypeptide of SEQ ID NO:69, also known as PRO357. Applicants are relying upon the gene amplification assay as providing utility and enablement for the claimed polypeptides.

At pages 119-137 of the specification, Example 28 discloses a gene amplification assay in which genomic DNA encoding PRO357 had a ΔCt value of at least 1.0 for fourteen out of fifteen lung tumor samples (93%) and twelve out of twenty-seven colon tumor samples (44%) when compared to a pooled control of blood DNA from several healthy volunteers. Example 28 asserts that gene amplification is associated with overexpression of the gene product (i.e., the polypeptide), indicating that the polypeptides are useful targets for therapeutic intervention in cancer and diagnostic determination of the presence of cancer (p. 119, lines 27-29). At page 121, ΔCt is defined as the threshold PCR cycle, or the cycle at which the reporter signal accumulates above the background level of fluorescence. The specification further indicates that ΔCt is used as a "quantitative measurement of the relative number of starting copies of a particular target sequence in a nucleic acid sample when comparing cancer DNA results to normal human DNA results." (pg. 121, lines 22-23). It is noted that at page 124, it is stated that samples are used if their values are within 1 Ct of the 'normal standard'. It is further noted that the ΔCt values at pages 125-127 are expressed (a) with values to one one-hundredth of a unit (e.g. 1.29), and (b) that very few values were obtained that were at least 2.

First, there are several problems with the data provided in this example. Only twelve out of the twenty-seven colon cancer samples tested positive. Therefore, if a sample were taken from an individual with colon cancer for diagnosis, ***it is more likely than not that this assay would yield a false negative result***. Second, even though the data in the specification has been corrected for aneuploidy using epicenter markers, and even if a majority of lung and colon tumor samples had tested positive, the data has no bearing on the utility of the claimed PRO357 *polypeptides*. In order for PRO357 polypeptides to be overexpressed in tumors, amplified genomic DNA would have to correlate with increased mRNA levels and increased polypeptide levels. No data

regarding PRO357 mRNA or PRO357 polypeptide levels in lung tumors have been brought forth on the record. The art discloses that a correlation between genomic DNA levels and mRNA levels cannot be presumed, nor can any correlation between genomic DNA levels and polypeptide levels. A specific example of the lack of correlation between genomic DNA amplification and increased mRNA expression is provided by Pennica et al. (1998, PNAS USA 95:14717-14722, cited on PTO-892 mailed 6/11/2003), who disclose that:

> "An analysis of *WISP*-1 gene amplification and expression in human colon tumors showed a correlation between DNA amplification and overexpression, whereas overexpression of *WISP*-3 RNA was seen in the absence of DNA amplification. In contrast, *WISP*-2 DNA was amplified in the colon tumors, but its mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient."

See p. 14722, second paragraph of left column; pp. 14720-14721, "Amplification and Aberrant Expression of *WISPs* in Human Colon Tumors." Another specific example is provided by Konopka et al. (Proc. Natl. Acad. Sci. (1986) 83:4049-4052, cited on PTO-892 mailed 1/12/2006), who state that "Protein expression is not related to amplification of the abl gene but to variation in the level of bcr-abl mRNA produced from a single Ph1 template" (see abstract).

Furthermore, Godbout et al. (J. Biol. Chem. 273(33):21161-21168, 1998, IDS filed 11/20/2006) speak to general lack of correlation between gene amplification and mRNA/protein overexpression. The abstract of Godbout teaches "The DEAD box gene, DDX1, is a putative RNA helicase that is co-amplified with MYCN in a subset of retinoblastoma (RB) and neuroblastoma (NB) tumors and cell lines. ***Although gene amplification usually involves hundreds to thousands of kilobase pairs of DNA, a number of studies suggest that co-amplified genes are only overexpressed if they provide a selective advantage to the cells in which they are amplified.***" (emphasis added). The protein encoded by the DDX gene *had been characterized* as being a putative RNA helicase, a type of enzyme that *would be expected to confer a selective*

advantage to the cells in which it (the DDX gene) was amplified. On page 21167, right column, first full paragraph, Godbout et al state "***It is generally accepted that co-amplified genes are not over-expressed unless they provide a selective growth advantage to the cell*** (48, 49). For example, although ERBA is closely linked to ERBB2 in breast cancer and both genes are commonly amplified in these tumors, ERBA is not overexpressed (48). Similarly, three genes mapping to 12q13-14 (CDK4, SAS and MDM2) are overexpressed in a high percentage of malignant gliomas showing amplification of this chromosomal region, while other genes mapping to this region (GADD153, GL1, and A2MR) are rarely overexpressed in gene-amplified malignant gliomas (50, 51). The first three genes are probably the main targets of the amplification process, while the latter three genes are probably incidentally included in the amplicons." (emphasis added). There is no evidence in the instant application that PRO357 confers any growth advantage to a cell, and thus it cannot be presumed that the protein is overexpressed because the genomic DNA including the gene being studied gene is amplified.

An additional reference that provides evidence that gene amplification does not generally lead to increased transcript is Li et al (Oncogene, 25:2628-2635, 2006). Li et al used a functional approach that integrated simultaneous genomic and transcript microarray, proteomics, and tissue microarray analyses to directly identify putative oncogenes in lung adenocarcinoma. On page 2633, right column, Li et al. state: "***In our study, 68.8% of the genes showing over-representation in the genome did not show elevated transcript levels***, implying that at least some of these genes are 'passenger' genes that are concurrently amplified because of their location with respect to amplicons but *lack biological relevance in terms of the development of lung adenocarcinoma*." Since more than half of the amplified genes were not overexpressed, Li et al constitutes strong evidence that ***it is more likely than not that gene amplification does NOT correlate with increased protein levels***, absent evidence that the protein has biological relevance in cancer. There is no such evidene for PRO357.

Therefore, data pertaining to PRO357 genomic DNA do not indicate anything significant regarding the claimed PRO357 polypeptides. The data do not support the specification's assertion that PRO357 polypeptides can be used as a cancer diagnostic agent. Significant further research would have been required of the skilled artisan to reasonably confirm that the claimed PRO357 polypeptides are overexpressed in any cancer to the extent that they could be used as cancer diagnostic agents, and thus the asserted utility is not substantial. In the absence of information regarding whether or not PRO357 polypeptide levels are also different between specific cancerous and normal tissues, the proposed use of the PRO357 **polypeptides** as diagnostic markers and therapeutic targets are simply starting points for further research and investigation into potential practical uses of the polypeptides. See Brenner v. Manson, 148 U.S.P.Q. 689 (Sup. Ct., 1966), wherein the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Response to Arguments

Applicants' arguments regarding U.S. Patent 7,208,308 are again acknowledged, however, Applicant is again reminded that each application is examined on its own merits, and the examiner is precluded from commenting on the '308 patent under 35 U.S.C. 282. It is noted that the '308 patent and the instant application do not claim the same subject matter, e.g., the polypeptide of SEQ ID NO:69.

Applicants' remarks that the PTO has acknowledged that a utility such as that asserted in the present application is sufficient by allowing or issuing various patents and applications (see pg. 5 of the reply). Applicants' remarks have been fully

considered but are not found persuasive. The instant application relies upon the gene amplification assay (Example 28) as providing utility and enablement for the claimed polypeptides, whereas each of the various patents and applications referenced by applicant rely upon microarray expression of mRNA correlated with polypeptide levels. As noted above the examiner no longer asserts that mRNA levels are not predictive of polypeptide levels. The basis of the instant rejections is solely that gene amplification levels are not predictive of mRNA or polypeptide levels. Applicants' attention is directed to USSN 09/941,992, which is also relies upon the gene amplification assay. Also see USSN 09/991,150.

Applicant reviews Example 28, and refers to the Goddard declaration as establishing that an amplification of at least 2-fold is significant and indicative of a cancer diagnostic marker. The Goddard declaration under 37 CFR 1.132 filed 06 November 2003 is insufficient to overcome the rejection of claims 27-34 based upon 35 U.S.C. §§ 101 and 112, first paragraph, as set forth above for the following reasons. In assessing the weight to be given expert testimony, the examiner may properly consider, among other things, the nature of the fact sought to be established, the strength of any opposing evidence, the interest of the expert in the outcome of the case, and the presence or absence of factual support for the expert's opinion. See Ex parte Simpson, 61 USPQ2d 1009 (BPAI 2001), Cf. Redac Int'l. Ltd. v. Lotus Development Corp., 81 F.3d 1576, 38 USPQ2d 1665 (Fed. Cir. 1996), Paragon Podiatry Lab., Inc. v. KLM Lab., Inc., 948 F.2d 1182, 25 USPQ2d 1561, (Fed. Cir. 1993). In the instant situation, the nature of the fact sought to be established is whether or not a $2^{1.05}$ to $2^{3.51}$-fold amplification of the gene encoding PRO357 in lung and colon tumors is significant. The significance can be questioned based on the absence of factual support for the expert's opinion. In the instant case, the facts are that fourteen of the fifteen lung tumor samples and twelve out of twenty-seven colon tumor samples did not show an amplification of the gene encoding PRO357, and the control used was not a matched non-tumor lung or colon sample but rather was a pooled DNA sample from blood of healthy subjects. The art uses matched tissue samples (see Pennica et al., Konopka et al.). This art, as well

as the Godbout et al and Li et al references cited above, constitute strong opposing evidence as to whether or not the claimed polypeptides have utility and enablement based on a presumption of overexpression in view of gene amplification data. Finally, while the Goddard Declaration speaks to the utility and enablement of genes, it does not speak to whether or not the encoded proteins are also found at increased levels in cancerous tissues. Since the claims under examination are directed to polypeptides, not genes, this question is critical.

Applicants' stance that it is more likely than not for amplified genes to have increased mRNA and protein levels because, in general, gene amplification increases mRNA expression and in turn, increased polypeptide levels is not found persuasive. Unlike the situations wherein a claimed compound has been tested and has shown a pharmacological activity and therefore has a therapeutic utility sufficient under the patent laws, or wherein an invention has only limited utility and is only operable in certain applications and therefore has some degree of utility sufficient for patentability, in the present situation Applicants have not provided any testing of PRO357 mRNA or PRO357 polypeptide expression. In the absence of any information on the role, activity or expression of the PRO357 polypeptide in cancer, the examiner therefore considers the asserted utilities to not be specific and substantial because the skilled artisan would not know if or how PRO357 polypeptide expression changes in cancer. Applicants' utility standard would mandate only a showing that it is "not implausible" that the invention will work for its intended purpose. If mere plausibility were the test for how to use a claimed invention, Applicants could obtain patent rights to "inventions" based on a disclosure consisting of little more than guesses as to the likelihood of their success. When one of the guesses later proved true, the "inventor" would be rewarded the spoils instead of the party who demonstrated that the method actually worked. A probable utility does not establish a practical utility, which is established by actual testing or where the utility can be "foretold with certainty." *Bindra v. Kelly*, 206 USPQ 570, 575 (Bd. Pat. Inter. 1979) (Reduction to practice was not established for an intermediate useful in the preparation of a second intermediate with a known utility in the preparation

of a pharmaceutical. The record established there was a high degree of probability of a successful preparation because one skilled in the art may have been motivated, in the sense of 35 U.S.C. 103, to prepare the second intermediate from the first intermediate. However, a strong probability of utility is not sufficient to establish practical utility.). Practical utility is a shorthand way of attributing "real-world" value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner, which provides some immediate benefit to the public. Applicants' remark's that the asserted utility does not involve either an inherently unbelievable undertaking or implausible scientific principles are acknowledged, however, credibility has never been questioned.

For these reasons, the rejection is maintained.

35 U.S.C. § 112, Second Paragraph

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

12. Claims 27, 30-31 and 33-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 27, 30-31 and 33-34 comprise the limitations that the polypeptide comprises the "extracellular domain", optionally lacking its associated signal peptide. The polypeptide of SEQ ID NO:69 identified as PRO357 is disclosed in Figure 26 to possess a single transmembrane domain, yet contains both N-myristoylation and glycosylation sites on the same side of the putative transmembrane domain, which makes it unclear what actually constitutes an extracellular domain, versus a cytoplasmic domain (which normally contains the N-myristoylation sites), if any such extracellular domain even exists. Further, according to Figure 26, the polypeptide contains N-myristoylation on both sides of the transmembrane domain. Therefore, it is unclear what is meant by the recitation of "extracellular domain" in the current claims.

Moreover, if the encoded polypeptide possesses an extracellular domain, the recitation of "the extracellular domain...lacking its associated signal sequence" is indefinite (e.g., claim 27, (d)), because a signal sequence is not generally considered to be part of an extracellular domain, in that signal sequences are cleaved from such domains during secretion from the cell.

13. Claims 27, 30-31 and 33-34 and are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (see MPEP 2163).

The claims are directed to isolated polypeptides comprising the extracellular domain of the polypeptide of SEQ ID NO:69, optionally lacking its associated signal peptide as well as said polypeptides fused to a heterologous polypeptide such as an epitope tag or an Fc region of an immunoglobulin. The transitional term "comprising" is open-ended or inclusive to the addition of unrecited elements (see MPEP 2111.03). The specification discloses that the amino acid sequence of SEQ ID NO:69 is 598 amino acids in length and is encoded by a nucleic acid (DNA44804-1248) that is amplified in lung or colon tumors compared to control DNA that appears to be from normal human blood (see Figs. 25-26, and pp. 119-137). However, the scope of the claims includes a genus of isolated polypeptides that comprise the amino acid

sequence of some undisclosed "extracellular domain" of SEQ ID NO:69 and chimeric polypeptides comprising such. The polypeptide of SEQ ID NO:69 identified as PRO357 is disclosed in Figure 26 to possess a single transmembrane domain, yet contains both N-myristoylation and glycosylation sites on the same side of the putative transmembrane domain, which makes it unclear what actually constitutes an extracellular domain, versus a cytoplasmic domain (which normally contains the N-myristoylation sites), if any such extracellular domain even exists. Further, according to Figure 26, the polypeptide contains N-myristoylation on both sides of the transmembrane domain. Figure 26 provides no written description of the extracellular domain, nor chimeric polypeptides comprising the extracellular domain. Thus, the claims embrace an extremely large genus of isolated polypeptides having disparate structures/sequences and functions and where the function of the polypeptide of SEQ ID NO:69 has not yet been identified.

Structural features that could distinguish a polypeptide in the genus from others in the class are missing from the disclosure and the claims. No common structural attributes identify the members of the genus and the genus is highly variable. The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general guidance is needed. Since the disclosure does not describe the common attributes or structural characteristics that identify members of the genus, and because the genus is highly variant, the characteristic of being encoded by a nucleic acid amplified in lung or colon tumors alone is insufficient to describe the genus of polypeptides that function equivalently. One of skill in the art would reasonably conclude that the disclosure of a single polypeptide, i.e., SEQ ID NO:69, does not provide a representative number of species of isolated polypeptides that minimally comprise some undisclosed and undefined "extracellular domain" of SEQ ID NO:69 to describe the claimed genus of polypeptides. As such, generic polypeptide sequences that are unrelated via structure and function are highly variant and not conveyed by way of written description by the specification at the time of filing. As such the specification lacks written description for the highly variant genus of polypeptides

and one skilled in the art would not recognize that applicants had possession of the genus of claimed polypeptides as instantly claimed.

Vas-Cath Inc. v. Mahurkar. 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the ad to recognize that he or she) invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is pad of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddles v. Baird, 30 USPQ2d 1481 at 1483. In Fiddles, claims directed to mammalian FGF'S were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence of SEQ ID NO:69, optionally lacking its associated signal peptide, but not the full breadth of the claim meets the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

14. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571)

272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643